

9.0 MECHANISMS OF INTERACTION

SUMMARY

Heating effects of microwave radiation are reasonably well understood and lead to significant physiological effects. Difficulties exist in determining the *in situ* heating in relation to applied dose due to the heterogeneous nature of body tissues. However, non-thermal subtle effects are considerably more difficult to recognise and understand.

It has been suggested that non-equilibrium processes are significant in the bioenergetics of living systems (Adey 1993), challenging the traditional approach of the chemistry of equilibrium thermodynamics. Rather than observing traditional dose-response effects, there have been a number of reports claiming both amplitude and frequency response "windows". The concept of an all-or-none effect at specific exposure conditions challenges conventional assumptions that the magnitude of a response increases with increasing "dose". If this can be reliably substantiated, it adds weight to the argument that there are significant as yet, unexplained, non-thermal mechanisms involved in biological effects of EMR. In recent years, a number of reports of effects of EMR have appeared which are incompatible with the concept of bulk heating and heat exchange. The altered flux of calcium ions across cell membranes has been commonly reported. The issue has not been resolved but the phenomenon may be due to molecular vibration of receptors rather than due to EM induced voltage activated effects (Moolenaar et al 1986; Hoth & Penner 1992) on channels in cell membranes.

Evidence exists that microwave radiation interacts directly with cell membranes to induce functional alterations in membrane components, including ATP-ase and ion channels. The role of free radicals is becoming appreciated from evidence of free-radical reactions in melanin-containing membranes leading to changes in membrane state. The reported effects are unexpected from the existing knowledge on physical interactions since they do not appear to be described by classical intensity- or dose- response relationships. It seems to be unlikely that a single biophysical interaction mechanism will be adequate to explain all of the reported non-thermal effects of RF and microwave radiation.

9.1 MECHANISMS

An important consideration in estimating the effects of dosimetry is the coupling of RF and microwave radiation to biological systems. This depends on the orientation of the subject (animal, human or culture vessel containing cells) relative to the field, and on its dimensions relative to the wavelength. Coupling to a body is maximal when its long axis is oriented parallel to the electric field and when its length is similar to the wavelength. Therefore, maximum (resonant) absorption for an exposed subject is frequency dependent and occurs at approximately 40 MHz for an average (electrically grounded) man, 600-700 MHz for a rat and 2500 MHz for a mouse whole body (Durney et al 1978).

It is well known that the distribution of RFR in an exposed object depends on many factors including frequency, orientation of exposure, dielectric constant of the constituent tissue. The design of experimental protocols is critical if the results are to provide meaningful extrapolation to a particular RF source. Cellular telephones are used in a specific manner. Most people would hold a phone to the same ear in the same orientation and proximity to the skull. Usually one would expect the antenna to be close to the parietal bone (although many airport officials have a peculiar habit of holding the large portable phones in front of their mouth so that they look across the top of the antenna). However, assuming normal usage patterns it would make sense to design experiments so that the RF source was located towards the lateral aspect of the skull. Chou et al (1985a) found significant differences in local SARs in eight different regions of the brain of rats and these all changed in each of seven different exposure arrangements. Lai et al (1984a) reported a difference in microwave response with pentobarbital depending on whether the rat was facing toward or away from the source of irradiation in a waveguide when the average whole body SAR remained constant; patterns of energy absorption in the brain differed substantially.

If the wavelength is smaller than the overall dimensions of the body, reflection and refraction of radiation at the interfaces of different tissues with different electrical properties, (air/skin boundary), can result in localised "energy hot spots". These hot spots can occur within the whole body at frequencies near body resonance, or within parts of the body such as the head at higher frequencies up to about 2-3 GHz. As frequencies increase and wavelengths decrease, power absorption per unit mass of tissue increases and penetration decreases. Above 10 GHz, absorption would be expected to be largely confined to the skin. When the

wavelength is larger than the exposed body, contact with other conducting bodies (including the earth) will cause induced electric currents to flow within the body and between the ground. Hot spots will be felt in regions of the body where the current flow is constricted by small cross-sectional areas, particularly in occupational exposures. Operators of RF sealer-welder equipment (13.5 or 27 MHz) have experienced SARs in the wrists and ankles above 20 W/kg while the SAR to the whole body may be approximately 0.4 W/kg (NRPB 1991).

Many of the biological effects of RF and microwave radiation which have significant implications for human health can be related to the induced heating. Heating from microwave and RF radiation best relates to SAR rather than to incident power density to account for differences in coupling. Temperature rise and specific energy absorption are related as shown:

$$T = J / (htc \times 4180)$$

where T = temperature rise (°C), J = specific energy absorption (J/kg) and htc = relative heat capacity (= 0.85).

This simple worst case situation neglects the effects of cooling. However, as a "rule of thumb" a SAR of 5 W/kg applied for one hour would increase temperature by 5°C. Localised heat may be dissipated by the blood through thermoregulatory processes, although the rate of cooling varies considerably for different organs and tissues. Temperature is profoundly affected by many factors which may confound interpretation of results from different experiments. The degree of thermal stress imposed on an animal (or human) by a given SAR is strongly affected by ambient temperature, relative humidity and air flow. The induced thermal load would be expected to increase with increasing body mass, at least in small animals. Some argument for a conservative extrapolation of effects from laboratory animals to humans comes from the observed differences in responses of mice and rats in haematology, immunology, reproduction and development (Gordon 1987; Gordon & Ferguson 1984). The difference in the ability of different species to regulate body temperature is a further confounding factor.

It would be unnecessarily simplistic to assume that bulk heating occurred evenly over body tissues and fluids and that it is the only mechanism that can result in a significant effect. Exposure conditions in an RF microwave field are altered considerably by the presence of an object which can profoundly perturb the field, depending on its size, orientation and electrical properties. Refractions and

differential absorption within a biological system can result in very complex non-uniform field distributions, and energy deposition. Transmitted energy can be focussed to very localised sites within a body organ. Absorbed RF energy can be converted to other forms of energy and interfere with the function of biological systems. While most of the energy is converted into heat, this does not provide an adequate explanation for a number of biological effects associated with exposures to low level EM radiations.

Evidence of a detectable response to minute temperature increase comes from the observations of human perception of pulsed RF fields. The rapid rate of temperature increase has been attributed to the phenomenon of thermoelastic expansion of brain tissue. This effect creates a response through an auditory pathway. At the cellular level, there is a large body of data on cell membrane responses which has developed the concept of a signal transduction pathway modifying cell behaviour following stimulation by low level microwave fields that do not produce a measurable temperature rise.

It has been suggested that the resonant excitation of particular molecules may elicit specific biological effects that are independent of heating. At frequencies between 1 and 10 GHz, there have been reports for and against resonant absorption of microwave energy by DNA molecules producing mechanical vibration in the DNA (Edwards et al 1984; Gabriel et al 1987, 1989). Based on evidence of the effects of amplitude-modulated radiofrequency fields in different biological endpoints, it has been suggested (Adey 1983, 1989), that co-operative interactions on the surface of cell membranes may allow weak fields to influence cellular processes through signal amplification and transduction processes.

Possible Non-thermal Mechanisms

There are difficulties encountered in attempting to ascribe acceptable mechanisms for the observed non-thermal effects of RF (and ELF) radiation. The process has been impeded for the following reasons:

- 1) Bioeffects are reported under conditions where the apparent coupling of energy to the biological system is significantly less than that required by classical physical-or physicochemical-interaction mechanisms,
- 2) Some biological effects occur over a limited range ("windows") of frequencies or modulations,

3) Some biological effects have been reported to occur in multiple dose or intensity ranges, referred to as intensity windows, instead of showing classical dose-response relationships.

A theory to adequately explain EMR bioeffects must incorporate a biophysical-interaction mechanism consistent with modulation- and intensity-windowed responses, occurring under conditions of low-field-energy coupling to living systems.

It is claimed (Cleary 1990) that there is unambiguous evidence of direct effects of RF and microwave radiation from the results of *in vitro* studies. Effects include, altered cell proliferation, cell membrane receptor and mediated events, and alterations in membrane channels. Although detailed biophysical interaction mechanisms for these effects are not currently available, it is considered that interactions at the microscopic level are related to the dielectric properties of biomacromolecules and molecular assemblages in the form of membrane receptor units, ion channels and enzyme complexes.

Membrane Ordering

There is evidence from various studies of microwave frequencies to demonstrate a direct effect on the cell membrane that may be due to alteration of the membrane molecular composition. Evidence of direct interactions at the molecular level comes from results of studies on transmembrane ionic fluxes and Na^+/K^+ ATP -ase catalytic activity. The direct effect of microwave interaction is restricted to a limited temperature range, implicating the involvement of membrane lipid phase transition (Liburdy 1992, 1994).

A theoretical model was proposed (Robertson & Astumian 1992) of the effect of alternating electric fields on reaction rates of membrane-associated enzyme molecules, induced by conformational change. The process has been termed electroconformational coupling. The model describes field-induced alteration in enzyme (ATP-ase) activity due to the resonant coupling of the electric field to an oscillatory activation - energy barrier of the enzymatic reaction. The model predicts effects on Na^+/K^+ ATP -ase inhibition by RF radiation in frequency windows, but not amplitude windows.

Investigation of the possible role of melanin and free radicals in cell membranes (Phelan et al 1992) provided some interesting data. Radiation with 2.45 GHz pulsed wave, SAR 0.2 W/kg was applied to melanin-containing cells and liposomes. Exposure of B16 melanoma cells for 1 h changed membrane

ordering, as measured by electron-paramagnetic-resonance (EPR) spectroscopy. Microwave exposure caused a shift from a fluid-like phase to a more solid or ordered membrane state. Similar results were obtained with liposomes that contained melanin, a redox polymer. Neither amelanotic B16 melanoma cells or liposomes exhibited the microwave-facilitated increase in membrane ordering. The microwave effect was inhibited by the free-radical scavenging agent superoxide dismutase (SOD), leading the authors to conclude that the microwave effect was mediated by the generation of oxygen radicals.

The results provide evidence of a direct specific microwave effect on a cell membrane that is dependent upon membrane composition. Changes in membrane order are known to alter the function of integral membrane proteins, such as ATP -ase, as well as membrane permeability. Consequently, microwave-induced membrane order could have physiological implications. The effect of microwave radiation on membrane order required the presence of melanin in this study. Other studies of microwave effects on Na^+/K^+ ATP -ase in the absence of melanin, as reviewed above, suggest the possibility of similar changes in membrane order that were related to temperature. The possibility that microwave radiation may exert a general effect on membrane order as mediated by temperature-dependent generation of oxygen radicals is supported by the results of Liburdy & Vanek (1985), who reported that temperature-dependent effects of microwave radiation on red-cell membrane permeability are dependent upon oxygen tension and the presence of antioxidants.

Thus the importance of free radicals in membrane-mediated effects of microwave radiation are becoming more widely accepted as a significant factor.

Other Evidence Of Direct Interaction

Additional evidence of a direct effect of microwave radiation on biomembranes was reported by Bolshakov and Alekseev (1992). Exposure of molluscan neurons to pulse-modulated (PM) 900 MHz microwave radiation caused increased rates of rapid, burst-like changes in firing rates. The threshold for the effect was 0.5 W/kg. Continuous wave (cw) radiation did not affect the firing rate at equivalent SARs. Mediator-induced activation of acetyl-choline, dopamine, serotonin, or gamma-aminobutyric acid (GABA) receptors was unaffected by either PW or CW microwave radiation, suggesting a direct effect of the microwave exposure on neuronal membranes.

Resonant Frequency Effects

An early publication that created a great deal of interest reported cell killing at specific frequencies in the GHz range (Grundler et al 1978). Strangely, although this work has frequently been used as an example of the peculiar phenomenon of frequency windows, there has been little work to either verify the effect or to investigate the mechanism. The feeling amongst the scientific community is divided, although there is some scepticism of the effect, nevertheless, the researchers are highly regarded.

A similar status applies to the report of enhanced, resonant absorption of microwaves by DNA molecules (Edwards et al 1984) in the 1 to 10 GHz frequency range. The reported effect could have implications to genetic effects from microwave exposure. Again, although this was a significant finding, it was some time before an attempt was made to duplicate the study. However, when it was tested (Gabriel et al 1987) the authors carried out duplicate tests on the dielectric properties of the same type of plasmid DNA in two separate laboratories. A reference sample was used to normalise the data against water and avoid recording artefacts from impedance mismatch within the system. The attempted verification failed to achieve the reported result. It is suggested that the effect may have been due to a measurement artefact. However, a recent report of possible rearrangement of brain tissue DNA (measured electrophoretically) following low level microwave exposure (Sarkar et al 1994) may keep the debate alive for some time.

The enhancement of the effect involving corneal lesions when irradiation follows the application of the drug timolol maleate is an important finding. This may be particularly relevant to the upper GHz frequency range. It is possible that the presence of a film enhances energy coupling to the cornea and through differences in molecular composition an impedance mismatch occurs at the aqueous humour, resulting in concentrated deposition of energy in the ~ 2mm thick cornea. The authors suggest the involvement of free radicals.

9.2 INTERPRETATION OF DATA

There are some problems in accepting some of the reports of biological effects of EMR due to:

- a. absence of accepted mechanisms to explain the observed effects
- b. absence of a dose response in many studies
- c. absence of independently verified results because of inconsistencies in methodology and choice of experimental endpoints
- d. proposed theories of nonlinear mechanisms, without threshold values, are contrary to established, conventional biological concepts
- e. extrapolation of cell responses when grown in culture to a potential health effect in organised human tissue
- f. so-called "windows" for effects at specified frequency or intensity

In terms of assessing human safety, it requires a quantum leap in philosophy to make a direct extrapolation of events occurring in a very simple biological system, such as yeast cell colonies, to the complex system of organised, differentiated adult tissue. Simple cell systems grown under controlled laboratory conditions provide a convenient and accepted method for studying fundamental processes in respiration, growth and behaviour, development and reproduction. The level of detail has extended to develop an understanding of molecular/biochemical pathways essential for normal cell growth. Thus, these systems are proven as useful test objects to establish interactive mechanisms, and many simple systems, including bacteria are routinely used in testing for toxicology and potential mutagenicity of environmental physical and chemical agents. The difficulty in extrapolation is primarily due to uncertainties about EMR exposure within the human body. The absence of an established mechanism for some of the non-thermal effects reported in cell systems creates difficulties in estimating its effect in organised tissue. Gradients in electric and magnetic fields, as well as in temperature, are quite different in cell culture (with single cell layer thickness or free cells in suspension) compared to large volumes of tissue in body organs.

The cell biology approaches involve standardised procedures to control variables as strictly as possible to allow detection of subtle effects. In this environment cell division is a constant and continuing process and the rate of growth is clearly defined for each species and strain. The rapid proliferation allows optimal opportunity to express developmental abnormalities through many generations on the way to produce neoplastic pathologies. It is not necessarily the case that

cells in developed human organs will be in active states of division when EMR exposure occurs. Thus, it is likely that an organ such as the adult human brain would be less sensitive to insult than cells growing in culture.

The attenuation of microwave energy by the scalp and skull increases as a function of frequency and is difficult to relate to exposure of cells in a highly absorbing liquid medium. It has even been suggested that the human head might act as some sort of a lens that concentrates radiated energy at certain frequencies, related to wavelength. The resonance frequency for the rat head is on the order of 5.0 GHz, while the human head is approximately two orders of magnitude larger with an equivalent difference in its resonant frequency.

It is clearly essential that dosimetry is accurately characterised for experiments (*in vitro* cells in liquid, and animals head volume) and human exposures before meaningful evaluation of human health implications can be achieved. In the meantime, data from cellular and animal studies should be seriously considered whether or not currently accepted and demonstrated mechanisms of action exist.

10.0 RF SAFETY GUIDELINES AND REGULATIONS

SUMMARY

A number of international standards exist and have similarities. There is some concern about basing standards solely on results of a few studies on behavioural changes mediated through a significant increase in temperature of the whole body. The data base for more sensitive effects is equivocal and rather inadequate. The 7W exclusion clause for mobile telephones is considered to be inappropriate and measures are currently being adopted for its deletion from the ICNIRP standard. The German Radiation Protection regulations differ from others in that it requires data for the absolute worst-case exposure condition, regardless of whether or not it represents normal use of the device. They were first to drop the 7W exclusion clause for cellular phones.

10.1 EMR EXPOSURE GUIDELINES

Initiatives of the Commission of the European Communities

The Commission of the European Communities (EC) has proposed limits of exposure in the workplace for non-ionizing radiations through its Directorate General (DG) V (Health and Safety) (CEC, 1992). The proposed limits for electric and magnetic fields are intended as a European Council Directive on the minimum safety and health requirements regarding the exposure of workers to the risks arising from physical agents.

DG XIII of the European Commission (Directorate General Telecommunications Information Industry Innovation) has mandated the European Committee for Electromechanical Standardisation (CENELEC) to prepare an exposure standard for the protection of people against electromagnetic fields. The work is being carried out by CENELEC technical committee TC111 "Human exposure to electromagnetic fields" and its subcommittees. DG XI has also initiated a COST (European Cooperation in the Field of Scientific and Technical Research) project on "Biological effects of electromagnetic fields". This provides a forum for technical and scientific cooperation between nineteen European countries and various research fields. The bioeffects project (COST 244) was established to study exposure of people to electromagnetic fields associated with communication systems at frequencies from DC to 300 GHz to foster exchange of information on biological research, epidemiology, and dosimetry within Europe. This arrangement has been criticised because of the absence of any organised peer-

review system to control the dissemination of information. A number of national and international bodies have published, or are currently developing standards (i.e. guidance and/or regulation) for safety of human exposure to electromagnetic fields.

The standards/guidelines include:

The international Commission for Non-Ionizing Radiation Protection (ICNIRP) of the International Radiation Protection Association (IRPA) for static magnetic fields and time-varying electric and magnetic fields at 50/60 Hz and between 100 kHz and 300 GHz (INIRC 1991).

The American Institute of Electrical and Electronics Engineers (IEEE) and ANSI standard for safety levels with respect to human exposure to radiofrequency electromagnetic fields in the frequency range 30 kHz to 300 GHz, (IEEE 1991; ANSI 1992).

The Physical Agents Committee of the American Conference of Governmental Industrial Hygienists (ACGIH) "Threshold limit Values" (TLVs) for occupational exposure to static and time-varying electromagnetic fields of frequencies less than 300 GHz (ACGIH 1992).

The proposed European Council Directive on the minimum health and safety requirements regarding the exposure of workers to the risks arising from physical agents, for static electric and magnetic fields and time-varying fields of frequencies less than 300 GHz (CC 1992).

The guidelines are based on data from biological and dosimetric studies and studies on exposed populations. They apply equally to workers and to members of the public but not to people who are exposed to electromagnetic fields and radiation for medical or therapeutic purposes.

Electromagnetic interference with medical electronic devices, such as pacemakers, are effects which are not considered explicitly. Electrically or magnetically sensitive prosthetic medical devices may be adversely affected by levels of field strength below those advised by the guidelines for protection from exposure to humans. This rapidly developing topic is beyond the scope of the current report. The current standards apply restrictions on exposure to radiofrequency and microwave radiation to prevent adverse responses to increased heat load and elevated body temperature. There is some argument

that this approach is incomplete as it does not consider the large amount of bioeffects data resulting from non-thermal interactions.

As frequency increases, the depth of penetration of radiation in the human body decreases and energy deposition becomes more superficial. In the tens of GHz frequency range absorption of microwave energy occurs primarily in superficial layers of the skin and the cornea. It is then appropriate to quantify exposure by power flux density rather than SAR averaged over a broad expanse of a thin layer of skin. Guidelines do not effectively take account of differences in effectiveness of pulsed versus continuous wave radiofrequency and microwave radiations, or of nonlinear responses.

10.2 RF SAFETY GUIDELINES/REGULATIONS

The American National Standards Institute (ANSI) IEEE Standard for Safety levels with respect to human exposure to radiofrequency electromagnetic fields was recently revised (ANSI, 1992). In an uncontrolled environment in the frequency range 300 MHz to 6 GHz the permissible power density is 10 mW/cm^2 , although the duration of exposure limit is 6 min for frequencies below 3 GHz and reducing to 10 s at 300 GHz. There was a relaxation of power density limits (20 mW/cm^2 at 300 GHz) for partial body exposures, except for the eyes and testes, for uncontrolled environments. The partial body exposure allows power density of 4 mW/cm^2 for frequencies in the range of 300 MHz to 6 GHz.

In determining these levels the ANSI committee set as their criteria for bioeffects data base as "only peer-reviewed reports of studies at $\text{SAR} \leq 10 \text{ W/kg}$, which had received favourable engineering and biological validation,...". The findings of the Risk Assessment Working Group were that the existing ANSI 1982 base criterion for 4 W/kg remained.

10.2.1 ANSI Standard: Is it Appropriate?

Although the current standard was issued in 1992, the accompanying bibliography forming the data base for the development of the standard mostly dated from the early 1970's to early 1980's. Out of a total 60 references only 19 are on biological effects. There are only six references that post-date the 1982 ANSI publication. Four of the bioeffects papers deal with the single subject of microwave induced hearing sensation and were written by the same individual. The list of so-called peer-reviewed publications includes a number of proceedings of workshops and conferences. Nevertheless, an important study on

potential cancer production by chronic exposure to microwaves (Guy et al 1992) was not included, although the research had concluded many years earlier. Another long-term study has only been reported in a limited fashion (Toler) and has yet to be published.

Although there have been a few publications on long term studies of behavioural effects (D'Andrea & de Lorge 1990) these were not considered for the ANSI standard. Some of these studies were carried out at 918 MHz frequency and found a threshold SAR value around 2 W/kg for disruption of behavioural activities in male rats (Moe et al 1976; D'Andrea et al 1980; Lovely et al 1977, 1983). Effects observed included reduced food intake, decreased blood sugar level and some increased activity. The exposures were repeated daily for many weeks. Altered behaviour was reported in studies carried out at 2450 MHz frequency (cw) at SAR values from 0.14 W/kg (D'Andrea et al 1986; De Witt et al 1987) to 3.2 W/kg (Lovely et al 1983). In a review of the topic D'Andrea and de Lorge (1990) specify that the SAR threshold for significant behavioural effects from long-term exposure at 2450 MHz is between 0.4 - 0.7 W/kg, and at 915 MHz is between 0.9 - 2.0 W/kg. By comparison, short-term acute exposure behavioural changes were associated with a minimum whole-body temperature increase of at least 1°C from SARs approximately 4 W/kg.

It is interesting that although the bibliography extends back as far as 1950 so few publications were judged to meet the ANSI criteria. The rationale for the ANSI guideline is based on the absence of verified reports of injury or adverse effects on the health of humans who have been exposed to RF electromagnetic fields. The ANSI guideline is based on behavioural effects on laboratory animals which the committee assumes as being the most sensitive indicator of biological effects. (This view is not necessarily shared by all scientists, some of whom consider this to be a rather crude endpoint). Since the reported threshold for disruption of ongoing behaviour in non-human primates always exceeded a whole-body SAR of 4 W/kg, this value was adopted as the working threshold for unfavourable biological effects in human beings in the frequency range from 100 kHz to 300 GHz. Some biologists are concerned about the apparent reliance on thermal mechanism of biological response when responses at the cellular level would be more sensitive. A safety factor of 10 was applied to obtain a maximum permitted whole-body SAR of 0.4 W/kg. Perhaps this may account in some way for the uncertainties involved. This is also a response to an acute exposure. It would seem to be more appropriate to base the standard on the effects of low level chronic exposures.

The US Environmental Protection Agency (EPA) has voiced its objection to the proposed incorporation by the US Federal Communications Commission (FCC) of the ANSI Standard because of its use of gross effects as a criteria for safety.

Justification of the ANSI criteria is given as: "The disruption of a highly demanding operant task is a statistically reliable endpoint that is associated with whole-body SARs in a narrow range between 3.2 and 8.4 W/kg, despite considerable differences in carrier frequency (400 MHz to 5.8 GHz), species (rodents to rhesus monkeys), and exposure parameters (near and far-field, multi-path and planewave, cw- and pulsed-modulated)". The robust nature of this effect and the use of body temperature as an indicator illustrates that a substantial biological response is evoked. To put into perspective an increase in SAR value by a factor of three for a much smaller animal, the rat, results in circulatory collapse and is followed by death within 15 mins. The effect has been reported at frequencies of 1 and 10 GHz at SAR of 12 W/kg (Frei et al 1994) which was associated with a significant increase in body temperature, and at 35 GHz where colonic temperature was unchanged.

An important issue of the effect on SAR due to absorption as a function of increasing frequency was demonstrated by Gandhi (1990). Based on the premise that, due to the high loss tangent of water in the millimeter wave band (30 - 300 GHz) penetration into the body is restricted to 1 to 2 mm, Gandhi estimated resulting SAR for a given incident power density of 5 mW/cm². Increasing the frequency from 30 to 60 GHz resulted in an increased SAR from 65 to 138 W/kg. In a study on absorption in pregnant women, Fleming and Joyner (1992) modelled the anatomical geometry of a pregnant woman and found that their estimates of SAR exceeded the current exposure limits prescribed by IRPA, ANSI and SAA in certain circumstances. The results indicated that the specific absorption rate in the embryo or fetus exceeded the safety standard limits for the general population (uncontrolled) in the frequency ranges 80-100 MHz in early pregnancy and for 300-1500 MHz in late pregnancy when the pregnant mother is exposed to the occupational limit of 0.4 W/kg. The standard for the general population, non-occupational (uncontrolled) exposure is an SAR of 0.08 W/kg averaged over the body of the embryo or fetus. At frequencies of 900 and 1200 MHz the estimated SAR in the fetus exceeded by a factor of three the limit set by the ANSI standard.

10.2.2 Cellular Telephones

Exclusion Clause

The Australian Standard (SAA 1990) and the IRPA Standard (IRPA 1988) contain exclusions for devices that have output powers of less than 7 Watts and transmission frequencies of less than 1000 MHz. The two types of hand held mobile telephones currently used in Australia are:- (a) (AMPS) Advanced Mobile Phone Systems operating with a maximum radiated power of 600 mW and frequencies between 825 and 845 MHz (b) (GSM) Global System Mobile with voice information digitally encoded radiates 0.8 and 2.0 W peak power in a frequency band 890 to 915 MHz. The transmission is pulsed at a repetition frequency of 217 Hz with pulse widths of approximately 0.6ms. Therefore, these hand-held mobile telephones are excluded from compliance with the Australian or international, IRPA, standard. Germany has dropped the exclusion clause and instead requires certification of compliance based on "worst case" spatial peak SAR, as exposures from "low power hand held devices has been strongly underestimated in the past" (Kuster 1993). The ICNIRP standard is about to be amended following agreement to delete the exclusion clause.

Pulsing Effects

The GSM digital telephones have stronger peak electromagnetic fields than the analogue telephones and have been shown to cause electromagnetic interference in a range of electronic medical equipment (Clifford et al 1994, Bassen et al 1994). Increasing the power of the GSM phone did not change the symptoms.

Many of the cellular responses, including transmembrane ionic flow, are elicited by RF emission that is modulated at around 100 Hz, whereas exposure to continuous wave at the same fundamental RF frequency has no effect. There may be some reason to consider that the relatively high instantaneous power that causes EM interference may be the parameter that elicits responses in sensitive biological cell membrane receptors. This issue of critical exposure parameters is fundamental to an evaluation of potential health issues and requires urgent investigation. The process of investigating underlying mechanism of interaction has had little direct attention to date.

Dosimetry

A recent study in Australia (Fleming & Joyner 1992) assessed the RF radiation dose in a physical phantom of a human head when exposed to an AMPS Telecom cellular telephone. The telephone emitted 600 mW continuous wave radiated power which produced an average SAR of 0.7 W/kg in tissue-equivalent gel within the eye. At the same distance of 5 cm from the antenna the measured power density was 0.27 mW/cm². No increase in temperature was detected. Using numerical estimates the same group (Fleming 1994) reported peak SAR of 1.77 W/kg /W in the skin muscle and bone adjacent to the ear.

Information received from the CTIA shows similar estimates *in situ* from cellular telephones used in the USA. Balzano was reported to have tested cellular phones with a physical model designed to give a worst-case estimate. In the model, signal attenuates rapidly, and the peak areas of energy absorption occurred in the cheek and mastoid area with peak exposures of 0.5 W/kg and brain exposures of 0.3 - 0.4 W/kg. When the antenna was collapsed the peak exposure was 1.1 W/kg and the brain exposure was 0.5 W/kg. Energy can be absorbed from near field, as well as far field, and the absorbed energy is a function of the medium, as well as geometry.

Gandhi originally described the anatomy of SAR from cellular telephone exposures using a magnetic resonance imaging model of a male volunteer. The average SAR of the whole body was less than 0.08 W/kg with a peak of 0.7 W/kg at the level of the handset. Approximately 10-12% of the power is absorbed in the head and neck region. The peak SAR (behind the ear) for any 1 gram of tissue was approximately 0.2 W/kg, and the average for brain tissue was 0.014 W/kg. However, other groups including NRPB and Kings College in the UK and Swiss Federal Institute of Technology have used numerical models and direct measurement to show substantially greater values for SAR in the brain when a cellular phone is located next to the head. The UK groups have greatly refined the procedure of MRI based phantom and numerical techniques to obtain resolution for dielectric constants for specific tissues (Gabriel et al 1999; Dimbylow 1993). It seems that an error in Gandhi's model was partly due to incorrect estimate of the dielectric constants for bone and brain tissue. Using FDTD calculations on 5×10^5 cells in 2 mm³ voxels in an MRI acquired image of a human head, Dimbylow (1994 BEMS presentation) showed SAR values 3.1 W/kg averaged over 10 gm tissue inside the head. The SAR averaged over 1 gm of tissue was 4.7 W/kg for a quarter wave monopole operating at 900 MHz. When

operating at 1.8 GHz the maximum SAR values along the side of the head were 4.6 and 7.7 W/kg for 10 and 1 gm of tissue, respectively. Based on these estimated SARs the maximum power that would be required to be emitted to meet the ANSI Safety Standard for the uncontrolled population (1.6 W/kg) would be 0.34 W at 900 MHz. For 1.8 GHz the maximum power value required to reach the ANSI safety limit is 0.21 W.

Lovisolo et al (1994) reported estimated SAR values of 1.9 W/kg averaged over 10 gm of liquid brain-equivalent material in a cylindrical phantom head exposed to 0.6 W cellular phone operating at 900 MHz. Using data supplied by Gabriel an anatomically correct (in terms of dielectric properties and dimensions) phantom head was used for the direct measurement of the worst-case exposure (Meire & Kuster 1994) as it was claimed that many cellular phones exceed the ANSI Standard for SAR per 1 gm of tissue. Their measurement show peak SAR levels of 3.5 and 2.5 W/kg at depths in the head of 5 and 10 mm, respectively. Bone of 5 mm thickness reduced SAR by less than 15%.

10.3 REGULATION

While cellular telephones on the market do meet an existing ANSI standard, FDA questions the adequacy of the standard.

FDA administers the Radiation Control for Health and Safety Act. Its purpose is to protect the public from unnecessary radiation from electric devices, and it covers many consumer products. Unlike the situation for medical devices, there is no premarket screening. FDA acts after marketing by recalling products, issuing civil penalties, and setting performance standards. Currently, there are insufficient data to establish cellular telephones as hazardous or to even set a safe standard. If FDA did have to go through notice and comment to set a new standard, it likely would be below today's ANSI standard (personal communication).

FDA needs research data that characterises the potential hazards, if any, of cellular telephone use as soon as possible, including emissions, biological effects and risks.

11.0 DOSIMETRY

Basic Concepts

Time-varying electric and magnetic fields induce electric fields and electric currents in conducting materials, including biological tissues. In general, biological effects depend on the strength of induced current and fields, although effects have been observed that appear to depend on other parameters. These effects are still not well understood and if they are confirmed, appropriate dosimetry may need to be developed.

Given the complex shape and non-homogeneous character of biological systems, it is exceedingly difficult to characterize completely the propagation of electromagnetic fields in the human body. The strength of the field reaching subcutaneous tissue is partly determined by absorption in the outer layers and by the reflection at the interface between different media. The amplitude of the electric and magnetic fields decreases exponentially with distance. The penetration depth of the field (∂) is defined as the distance at which the field is attenuated by a factor of $e^{-1} = 0.368$. It decreases with increasing frequency according to the equation:

$$\partial = 1/(\sqrt{\pi f s \mu_0})$$

where f is the frequency, μ_0 is the permeability of the free space (1.26×10^{-6} H/m) and s is the conductivity of the medium. The last quantity, in turn, depends on the frequency.

The penetration depths of high-water-content biological medium at various frequencies are given below:

| f (MHz) | s (S/m) | ∂ (mm) |
|-----------|-----------|-----------------|
| 10 | 0.625 | 200 |
| 100 | 0.889 | 53 |
| 300 | 1.37 | 25 |
| 915 | 1.6 | 13 |
| 2450 | 2.21 | 6.8 |
| 3000 | 2.26 | 6.1 |
| 5000 | 3.92 | 3.6 |
| 10000 | 10.3 | 1.6 |

In the radiofrequency band, two quantities are commonly used to quantify the interaction between the field and the biologic medium, ie the current density (used predominantly at frequencies below 100 kHz) and the specific absorption rate (SAR). The latter describes the rate at which radiant energy is deposited into a unit mass of tissue and is usually expressed in units of W/kg. The current density can be usefully compared to those known to produce physiological responses (eg muscle stimulation) or to endogenous body currents.

The interaction between radiant energy and an absorbing medium is particularly efficient when the dimension of the medium is equal, or approximately equal, to a multiple of $1/2$ the wavelength (resonance condition). Therefore, the peak absorption for an adult man exposed to a wave with the electric field parallel to the length of the body, occurs at about 75 MHz. The head resonates at much higher frequencies (≈ 1 GHz).

At higher frequencies, the basic interaction mechanism is the rotation of molecules in which positive and negative charges are separated in space (polar molecules). The most common such molecule in biological matter is water. Polar molecules tend to align themselves with the electric field and, as this oscillates, they tend to follow these oscillations. In this process energy is dissipated in the form of heat. The resulting increase in temperature (ΔT) measured in $^{\circ}\text{K}$ can be expressed as $\Delta T = (\text{SAR} - \text{HLR})t/C$, where HLR is the rate of heat loss per unit mass, due to thermal conduction and convection, and t is the time in seconds.

The SAR is not readily measurable in practice, therefore in order to prevent overexposure, it is necessary to resort to published data that relate the SAR to the electric and magnetic field strengths or the power density of the incidence radiation.

The SAR can be determined empirically or theoretically. Both of these methods have limitations and rely on each other for validation and complementation. Computational methods indicate that the SAR is a function of frequency, of the wave polarization and that it peaks at resonant frequencies.

With respect to the absorption characteristics of the human body, the RF range can be divided into four regions

- up to 30 MHz (sub-resonance range), radiation incident on the trunk is predominantly absorbed at the surface, whereas that incident on the legs and neck may result in significant energy absorption. In this range, absorption increases rapidly with frequency.
- between 30 MHz and 300 MHz (resonance range), the SAR per unit incident power density reaches a peak, as resonance conditions are attained for the whole body and body parts.
- between about 400 MHz and 3 GHz (hot spot range), significant heating may occur in particular sites in the body. The size of these 'hot spots' decreases from several cm to about 1 cm as the frequency increases.
- for frequencies above about 3 GHz (surface absorption range), radiant energy is absorbed at, and heating is limited to, the surface of the body.

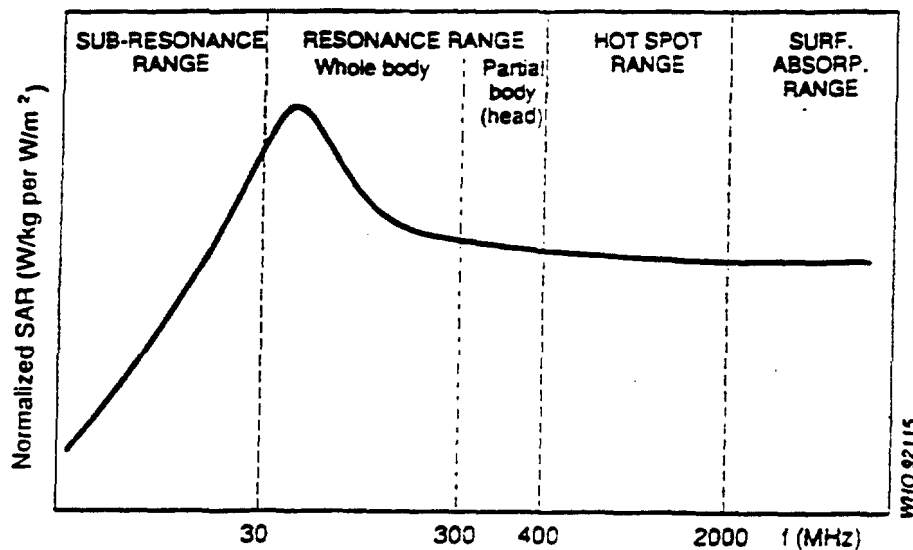


Fig. 11.1 Variation of normalised SAR with frequency and related absorption characteristics in living organisms. (from WHO, 1993)

It must be stressed that the above considerations depend on the body dimensions, therefore adequate allowance must be made when extrapolating results obtained by animal studies. For example, at 2450 MHz, the SAR resulting from exposure to 10 W/m^2 , with the E vector parallel to the long axis of the body is about 70 times higher for a mouse (whose length is comparable to the radiation's wavelengths) than for a man (Durney et al 1980).

SARs have also been empirically measured on human volunteers or on human models. For frequencies below and close to the resonant frequencies, experimental values exceeded the calculated values by factors of 3-4 (Hill 1984 a,b,c; Guy 1987).

A good agreement between calculated values and measurements in models were found for frequencies at and above the resonant frequency for irradiation in free space and with the electric field parallel to the long axis of the body.

The SAR is also affected by several practical exposure conditions (position of the body and of the limbs, distance from the ground, footwear etc). Using the results of these computations and measurements and including appropriate safety margins, limits to the maximum acceptable SAR or, as appropriate, maximum induced current density, are translated into maximum permissible exposure levels.

Within the context of the current concerns about brain tumors allegedly caused by exposure to RF radiation from cellular phones, it is interesting to examine the absorption properties of the brain itself and of the DNA molecule.

The brain is a tissue rich in water, but with a substantial proportion of fatty tissue. It has a conductivity at about 1 GHz of approximately 1.1 S/m and a penetration depth of approximately 1.5 cm. While the brain has a metabolic rate about 16 times higher than that of muscle tissue (and therefore generates much more heat than muscle tissue), this is more than compensated by 20-fold higher rate of blood flow and a somewhat higher thermal conductivity (Guy 1974). Therefore, brain tissue is no more prone to RF heating than muscle tissue.

There have been conflicting results on the question of resonant absorption of microwave radiation in DNA. Resonance absorption peaks were reported by Swicord et al (1983) and Edwards et al (1984, 1985). Zhang (1989) calculated that

resonance absorption of microwave energy in NA is possible in the GHz and sub-THz frequency ranges. The most recent reports, however (Foster et al 1987, Gabriel et al 1987 Maleev et 1987, Rhee et al 88, Garner et al (1990) , tend to argue against the presence of resonant absorption.

Current Issues

A new challenge has arisen recently, due to the relatively new situation of radiating antennae being routinely placed very close to the human body. Data calculated or measured in this condition are extremely dependent on the geometry of the model used.

Gandhi and co-workers used both computational and experimental techniques to obtain SARs in the human head for ten cellular phone from four different manufacturers. For their computations, they used a high resolution model consisting of very small cells (2x2x3 mm) each having appropriately defined properties reflecting their anatomical equivalent. The computation results were verified using an head-shaped model made of tissue equivalent materials. By contrast, Balzano (1994) and Kuster (1993) used a much cruder approach, relying on a head-shaped mannequin filled with a solution that simulates brain tissue and, approximately, bone and fatty tissue.

Gandhi's results were summarized as follows:

| | |
|---------------------------------------|------------------|
| peak SAR over any 1 g of tissue | 0.09 - 0.29 W/kg |
| peak SAR over any 1 g of brain tissue | 0.04 - 0.17 W/kg |
| whole body SAR | 0.5 - 1.1 mW/kg |

The highest SAR were found to occur in tissue in the upper ear.

These figures contrast sharply with those obtained by Balzano et al (1994) and Meier and Kuster (1993), although the phones output power was the same in all cases (0.6 W).

Balzano et al (1994) measured the SAR induced in human-equivalent phantoms by two types of Motorola cellular phones. They found SARs as high as 1.4 W/kg for "Flip" phones (ie phones with a very thin radio case and a collapsible antenna; when the antenna is extended, the radiation emitted is slightly further away from the head and this results in lower SARs).

| | | |
|------------------|-------------------|----------------|
| "Classic" phones | Peak SAR | 0.2 - 0.4 W/kg |
| "Flip" phones | Antenna collapsed | 0.8 - 1.4 W/kg |
| | Antenna extended | 0.6 - 1.0 W/kg |

SARs of up to 1.7 W/kg were measured by Kuster et al (1993) under "standard" conditions and SARs as high as 5.3 W/kg under "worst case" conditions, with the antenna actually touching the head.

Mokhtech et al (1994, BEMS Newsletter March/Apr p8), also reported that local peak SARs exceeding the ANSI safety limits may be encountered.

Meier and Kuster (1993) argue that "anatomically correct shell phantoms [such as that used by Gandhi] have been proven poorly suitable to achieve good reproducibility because the position of the radio with respect to the phantom is difficult to define". Their and Balzano's approach is of determining the SAR under 'worst case conditions'.

Which of the two approaches is more appropriate is as much a political as a scientific decision. From a technical view point, the main concern is the view expressed by Balzano (quoted in Microwave News, Jan/Feb 1994, p 13) that Gandhi's results were not obtained by pressing the phone against the ear. At the time of writing, details of Gandhi's measurements have not yet appeared in the scientific literature. If Balzano's claim is correct, it casts some doubt on the usefulness of Gandhi's results. Kuster also suggests that "for some cellular phones, it is not unusual for the antenna to touch the skull" (Microwave News, Jan/Feb 1994, p 14). Nevertheless, even Kuster's results indicate that the majority of the phones tested complied with the ANSI/IEEE C95.1 Standard (and consequently, with the Australian/New Zealand Standard), when the phones are tested under standard conditions. When tested under worst-case conditions (ie with the antenna touching the head), they all exceeded the limit, with 2 of the 6 models tested¹ being about 50% above the recommended limit.

¹The units tested by Kuster or Gandhi were not identified, therefore it is not clear whether these models that produce SARs clearly exceeding the limit are available in Australia or indeed are on the market. Motorola use the 1.6 W/Kg SAR measured under Balzano's 'worst-case' testing as a 'pass or fail' criterion for their phones (Balzano 1994).

In order to ensure compliance with safety limits, it is necessary that testing conditions be reproducible. The requirement that compliance be demonstrated under "worst case conditions" overcomes some of the standardization problems, such as the position of the hand holding the phone. In "worst case" tests, the telephone is supported against the head by a non-conducting prop. In practice, the presence of the hand reduces the SAR measured in the head.

The question of low-level dosimetry has been given very little consideration to date. The evidence of non-thermal effects is very complex to interpret and generalize. WHO (1993) suggest that the SAR may also provide a valid measure of all intensity dependent interaction mechanisms, although some additional information may be required, such as modulation characteristics and amplitude "windows" that are biologically active. However, at this stage, it is difficult to see how these additional characteristics could be defined and even whether the observed non-thermal effects are intensity dependent.

For the purpose of further research on human subjects, "dose" or "exposure" need to be defined not necessarily in rigorous, biologically validated terms, but at least in terms that will allow to identify reliably 'cohorts' of subjects whose exposure conditions are clearly different from that of the general population and, preferably, to establish an exposure gradient. The most obvious, but not necessarily accurate, tentative definition of exposure is the time-weighted average of the field power density.

For each of these tentative definitions, the following questions need to be addressed and answered:

- how is 'exposure' distributed among the community?
- how is 'exposure' distributed among specified occupational groups?
- what attributes can be used as 'proxy' for exposure? (eg occupational title, proximity to specific sources etc)
- how strong is the association between a proxy and the 'exposure'?
- if proxies are used, what is the likely effect of inaccurate exposure assessment on the results of the study?
- are any of these proxies associated with other possible risk factors (eg chemical carcinogens, other EMR frequencies) that may confound the results of new studies?

12.0 EPIDEMIOLOGY

Epidemiology is the study of the occurrence of disease in relation to factors affecting the individual, his environment and his lifestyle. Epidemiology may be used to infer a causal link between these factors and the disease, although the biological mechanism responsible may not be identified. This, however is a difficult and often controversial process. To help distinguish causal from non-causal associations, Hill (1965) suggested nine criteria:

- 1) strength of the association,
- 2) consistency,
- 3) specificity,
- 4) temporality,
- 5) biological gradient,
- 6) plausibility,
- 7) coherence,
- 8) experimental evidence, and
- 9) analogy.

However, meeting these criteria need not be seen as necessary prerequisite to accept the association as causal (Rothman 1986). In particular, criterion 3 (specificity), is regarded by Rothman as "useless and misleading" and experimental evidence is seldom available for human population. Hill himself admitted that "none of my nine viewpoints can bring indisputable evidence for or against the cause-and-effect hypothesis and none can be required as a *sine qua non*". Lanes (1985) argued that causal inference is not part of science, but a question for public policy. While this may be an extreme position, it highlights how this question is not easily addressed using rigorous scientific thought. However, it is incumbent upon the scientist to investigate how the quality of the study may have reflect upon Hill's criteria.

Epidemiological studies of exposure to radiofrequency radiation

A number of epidemiological studies have conducted among occupational groups believed to be exposed to above-average levels of RF radiation. Some studies have reported health effects consistent with the well understood thermal hazards. For example, RF levels in excess of the recommended limits have been measured in proximity of diathermy units used in physiotherapy (Stuchly et al